UNITED STATES PATENT & TRADEMARK OFFICE

Appl. No.	:	10/045,607
Applicant	:	Lino TAVARES et al.
Filed	:	October 23, 2001
A.U.	:	1615
Examiner	:	GHALI, Isis A D
For:	:	**LORATADINE TRANSDERMAL DEVICE AND METHODS**
Docket No.	:	208.1004US
Customer No.	:	23280

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

May 4, 2006

RESPONSE TO OFFICE COMMUNICATION

Sir:

In response to the Notification of Non-Compliant Appeal Brief mailed April 11, 2006, Appellants submit herewith a supplemental brief, in compliance with 37 CRF 41.37(c).

In response to section 4 of the April 11, 2006 Notice, Appellants note that a concise explanation of the subject matter defined in each of the independent claims involved in the appeal can be found at section V, pages 2-4 of the supplemental brief.

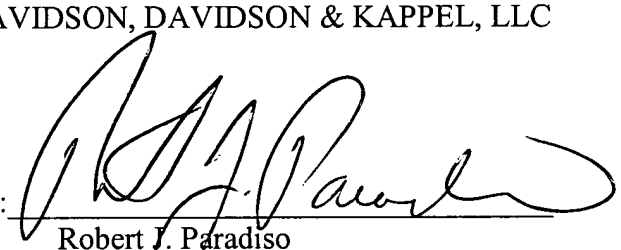
In response to section 9 of the April 11, 2006 Notice, an appendix indicating the decisions rendered by a court or the Board in the proceeding identified in the Related

Appeals and Interferences section can be found at section XI, page 22 of the supplemental brief.

In response to section 8 of the April 11, 2006 Notice, Copies of the evidence entered by the Examiner and relied upon by the Appellant in the appeal, along with a statement setting forth where in the record that evidence was entered by the Examiner can be found at section XII, page 23 of the supplemental brief.

Appellants submit that all defects, as listed in the April 11, 2006 Notice have been addressed and corrected. Prompt consideration of the arguments presented in the accompanying supplemental brief and reversal of the final rejections is earnestly solicited.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: 
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May 4, 2006

APPELLANTS SUPPLEMENTAL BRIEF ON APPEAL UNDER 37 C.F.R. §1.192, IN COMPLIANCE WITH 37 CFR 41.37(c)

Sir:

In response to the Notification of Non-Compliant Appeal Brief mailed April 11, 2006, Appellants submit this supplemental brief, in compliance with 37 CRF 41.37(c). A response to the April 11, 2006 Notification is due May 11, 2006. Accordingly, this supplemental brief is being timely filed.

Appellants submit this brief for the consideration of the Board of Patent Appeals and Interferences in support of their appeal of the Final Rejection dated July 28, 2005 in the above-identified application.

I. REAL PARTY IN INTEREST

The real party in interest is Purdue Pharma LP, having a place of business at One Stamford Forum, Stamford, Connecticut 06901-3431, assignee of the entire right, title and interest in the above-identified patent application.

II. RELATED APPEALS AND INTERFERENCES

Appellants and their legal representatives and assignee are not aware of any appeal or interference that directly affects, will be directly affected by, or will have a bearing on the decision in this appeal.

III. STATUS OF CLAIMS

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-49 are currently pending and are subject to a final rejection, dated July 28, 2005. Claims 1-7, 12, 15, 17-19, 21, 25-28, 31 and 39 were previously cancelled. This appeal is taken from this final rejection. Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-49 remain in the application and are appealed. A copy of these appealed claims is attached hereto as an Appendix.

IV. STATUS OF AMENDMENTS

In the Amendment under 37 C.F.R. § 1.111, dated May 9, 2005, claims 46-49 were added. Claims 1-7, 12, 15, 17-19, 21, 25-28, 31 and 39 were previously cancelled. The claims have not been amended after the Final Rejection of July 28, 2005.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A. Claim 8

Independent claim 8 recites a method for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with transdermal delivery systems containing loratadine. See specification, *e.g.*, at page 4, lines 20-22.

Claim 8 further recites in the method that the delivery system remains in contact with the skin of the patient for at least 5 days, and maintains an effective mean relative

release rate to provide a therapeutic blood level of loratadine within three days from the initiation of the dosing interval, and maintains a therapeutic blood level until the end of at least the five-day dosing interval. See specification, *e.g.*, at page 5, lines 15-21.

Claim 8 further recites specific plasma levels for the claimed method, namely a plasma level of loratadine at steady state from about 1 to about 3 ng/ml; see specification, *e.g.*, at page 6, lines 2-3, and recites a mean relative release rate, namely:

from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours; see specification, *e.g.*, at page 6, lines 22-23;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours; see specification, *e.g.*, at page 6, line 24;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours; see specification, *e.g.*, at page 6, line 25;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours, see specification, *e.g.*, at page. 9, lines 20.

The release rate, as specified in the method of claim 8 is determined via a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water. See specification, *e.g.*, at page 6, lines 26-27.

B. Claim 20

Independent claim 20 recites a transdermal delivery system containing loratadine which provides a mean relative release rate, namely:

from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours; see specification, *e.g.*, at page 6, lines 22-23;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours; see specification, *e.g.*, at page 6, line 24;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours; see specification, *e.g.*, at page 6, line 25; and

from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; see specification, *e.g.*, at page. 9, lines 20.

The release rates of the system recited in claim 20 is determined via a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water. See specification, *e.g.*, at page 6, lines 26-27.

Claim 20 further recites that the system is maintaining an effective mean relative release rate to provide a therapeutic blood level of loratadine within 36 hours from the initiation of the dosing interval, see specification, *e.g.*, at page 8, lines 31-33, and a plasma level of loratadine of at least about 0.1 ng/ml by about 6 hours after application. See specification, *e.g.*, at page 9, lines 2-3.

Claim 20 further recites that the system is maintaining a therapeutic blood until the end of at least a five-day dosing interval and a plasma level of loratadine at steady-state from about 1 to about 3 ng/ml, see specification, *e.g.*, at page 8, lines 28-34.

C. Claim 46

Independent claim 46 recites a method for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with transdermal delivery systems containing loratadine. See specification, *e.g.*, at page 4, lines 20-22.

Claim 46 further recites in the method that the delivery system remains in contact with the skin of the patient for at least 5 days, and maintains an effective mean relative release rate to provide a therapeutic blood level of loratadine within three days from the initiation of the dosing interval, and maintains a therapeutic blood level of until the end of at least the five-day dosing interval, and a plasma level of loratadine at steady-state from about 1 to about 3 ng/ml, see specification, *e.g.*, at page 5, lines 15-21 and at page 8, lines 28-34.

Claim 46 further recites in the method that the backing layer of the transdermal delivery device is substantially impermeable to the loratadine, and has a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine and 0.1 to 30% by weight of a solvent for the loratadine, see specification, *e.g.*, at page 11, lines 22-26.

Claim 46 further recites in the method that the transdermal delivery system containing loratadine provides a mean relative release rates, namely:

from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours; see specification, *e.g.*, at page 6, lines 22-23;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours; see specification, *e.g.*, at page 6, line 24;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours; see specification, *e.g.*, at page 6, line 25; and

from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; see specification, *e.g.*, at page. 9, lines 20.

The release rate, as specified in the method of claim 46 is determined via a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water. See specification, *e.g.*, at page 6, lines 26-27.

VI. SUMMARY OF INVENTION

The present invention is directed to transdermal delivery systems containing loratadine or a pharmaceutically acceptable salt thereof, or methods of using a transdermal delivery system, which provide (i) *specific* mean relative release rates as determined via an in-vitro permeation test and (ii) *specific* plasma levels when administered to a human patient.

In the following arguments, Appellants contrast this invention to the two remaining prior art references cited by the Examiner, which, to the extent that they teach

a transdermal delivery system of loratadine for the treatment of allergic conditions, fail to teach or suggest the specific pharmacokinetic parameters and release rates provided by the transdermal device of the present invention.

VII. ISSUES

The following issues are presented for appeal:

(1) Whether claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 are unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,910,205 to Kogan et al.

(2) Whether claims 37, 38, 44, and 45 are unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent 5,240,711 to Hille et al.

VIII. GROUPING OF CLAIMS

The Examiner has rejected claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 as a single group. However, Appellants believe that claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 may be divided into three (3) groups for appeal. As argued below, Appellants assert that these groups of claims are separately patentable, and the claims of each group stand or fall together.

Group I includes claims 8-11, 13, 14, 16 and 47 as a single group

Group II includes claims 20-24, 29, 30, 32-38, 40-45 and 48 as a single group.

Group III includes claims 46 and 49 as a single group.

Appellants believe that these groupings of claims are separately patentable, as the claims of Group I are directed to methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with transdermal delivery systems

containing loratadine; the claims of Group II are directed to transdermal delivery systems containing loratadine which provide certain release rates and certain plasma levels of loratadine; and the claims of Group III are directed to a method of treating seasonal allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering to a human patient loratadine transdermally wherein the transdermal delivery device includes a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof.

Appellants submit that the methods and devices of Groups I and II, respectively, can include materially different ingredients in the reservoir layer than the devices of the methods of Group III. For example, the methods of Group III recite a administering a transdermal delivery device containing loratadine or pharmaceutically acceptable salt thereof and including a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof, whereas the methods of the claims of Group I and the devices of the claims of Group II are not limited to only these ingredients in the reservoir.

Appellants believe that these three groups of claims are separately patentable.

IX. ARGUMENT

A. 35 U.S.C. § 103(a) Rejection of Claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, 40-49 Based on U.S. Patent No. 4,910,205 to Kogan et al.

1. The Examiner's rejection

The first issue presented is whether claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38 and 40-49 are unpatentable under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 4,910,205 to Kogan et al. ("Kogan").

In the Final Office Action, the Examiner asserted the following:

> [I]t would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal device to deliver loratadine to treat allergic conditions as disclosed by US '205, *and adjust the dose* to deliver a specific desired plasma profile according to the patient's need, motivated by the teachings of US '205 that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the condition being treated, with reasonable expectation of having a transdermal drug delivery device that delivers loratadine at the desired levels and treats allergic conditions effectively.

Final Office Action at page 4 (emphasis added).

2. U.S. Patent No. 4,910,205 does not render the claims obvious

Appellants respectfully submit that Kogan fails in the very least to teach or suggest the following claimed relative release rates recited in the present claims as determined by the Valia-Chien cell:

> said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;
>
> from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours

While the Valia-Chien cell might have been known to one skilled at the art at the time of the invention, the prior art is absolutely silent about the claimed relative release rates as determined by the Valia-Chien cell. Moreover, the prior art of record does not even apply the Valia-Chien cell to transdermal delivery systems containing loratadine. Thus, the prior art cited by the Examiner cannot teach or suggest specific mean relative release rates claimed in the present invention.

In the Final Office Action, the Examiner acknowledged that the Kogan "does not teach the specific delivery profile of loratadine, the specific amounts of different ingredients, or specific solvents and softening agents in the transdermal delivery system." Final Office Action at page 3 (*emphasis added*). The examiner also acknowledges that the prior art would need to be adjusted in order to deliver the claimed plasma profile. See Final Office Action at page 4. Accordingly, Appellants respectfully disagree with the Examiner's later position that "it is expected to have the same delivery profile from a transdermal delivery device disclosed by the prior art that has the same composition and the same amount or loratadine." Id.

Appellants further submit that the Examiner relied on impermissible hindsight vision in reconstructing the present invention. The Examiner stated that it is "within the skill in the art to select optimal parameters in order to achieve a beneficial effect," Final Office Action at page 3. The Examiner also asserted that "motivation to modify the dose would have been driven from the teaching of US '205 that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the conditions being treated, with reasonable expectation of having a transdermal drug delivery device that delivers loratadine at the desired levels and treats allergic conditions effectively." Final Office Action at page 6. However, the Examiner has failed to provide motivation to one skilled in the art to formulate a transdermal delivery system which

provides the specific relative in-vitro release rates and the specific blood plasma level recited in the present claims, and has also failed to provide motivation to one skilled in the art to utilize the methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with such transdermal delivery systems. It is respectfully submitted that only in view of the teachings of the present application would one of ordinary skill in the art be motivated to formulate the transdermal delivery systems or utilize the methods of treatment as recited in the present claims.

As the Examiner has failed to provide motivation to manipulate the prior art in order to arrive at either the claimed transdermal delivery systems containing loratadine or the claimed methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with such transdermal delivery systems, Appellants respectfully request that the obviousness rejection over Kogan be withdrawn.

Appellants note that the release rates as determined by the Valia-Chien cell recited in the claims are limitations of the transdermal delivery systems and methods of the present claims. Further, Appellants respectfully submit that "[a] functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used." MPEP 2173.05(g), Eighth Edition, Revision 2.

With respect to Group III, Appellants respectfully submit that claim 46, which recites in part, "a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof" (*emphasis added*), is separately patentable over Kogan et al. Appellants respectfully submit that Kogan is directed to the surprising result provided by a loratadine transdermal device which contains a combination of a volatile solvent, an essential oil and a fatty acid ester. See Kogan et al., col. 1, lines 54-59. Therefore, after reading Kogan, one skilled in the art would not be motivated to

utilize a device that does not contain an essential oil, such as the system as recited in independent claim 46. Thus, claim 46, and Group III is patentable over Kogan.

For the foregoing reasons, Appellants believe that independent claims 8, 20 and 46 are patentable over Kogan and respectfully request that 35 U.S.C. § 103 (a) rejection over these claims be reversed. As claims 9-11, 13, 14, 16, 21-24, 29, 30, 32-38, 40-45, and 47-49 depend from either independent claim 8, 20 or 46, and include all the limitations of the independent claim they depend on, Appellants submit that the rejections of these dependent claims should be reversed.

B. 35 U.S.C. §103 (a) Rejection of claims 37, 38, 44 and 45 Based on U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al.

Claims 37, 38, 44 and 45 were rejected under 35 U.S.C. § 103 (a) on the grounds of being unpatentable over Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. Claims 37, 38, 44 and 45 all depend from claim 23, which is dependent on claim 20.

1. The Examiner's rejection

The second issue presented is whether claims 37, 38, 44 and 45 are unpatentable under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent 5,240,711 to Hille et al. ("Hille").

In the Final Office Action, the Examiner stated the following:

> [I]t would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic conditions using a transdermal device comprising loratadine that provides a specific delivery profile and having particular structure as disclosed by US '205, *and select* the specific solvents and softening agents disclosed by US '711, motivated by the teaching of US '711 that the transdermal device having these particular ingredients in its reservoir layer provides a controlled delivery of the drug, with reasonable expectation of having a transdermal drug

delivery device to deliver loratadine to treat allergic conditions effectively.

Final Office Action at pages 7-8 (emphasis added).

2. U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. does not render the claims obvious

Appellants respectfully submit that Hille describes the use of burpenorphine as the active agent, and fails to teach or suggest the use of any other active agent, such as loratadine. Therefore, Appellants submit that Kogan and Hille are improperly combinable, as one of skill in the art would not look to combine a reference directed to the treatment of seasonal allergies with a reference directed to the treatment of pain.

Appellants additionally submit that even if the references were properly combinable, the Examiner is improperly picking and choosing a specific element of Kogan, i.e. loratadine, and combining it with the transdermal delivery device of Hille. One "...cannot pick and chose among the individual elements of assorted prior art references to recreate the claimed invention." Smith Kline Diagnostics, Inc. v. Helena Laboratories Corporation, 859 F. 2d 878, 887 (Fed. Cir. 1988).

Furthermore, Hille fails to cure the deficiencies of Kogan (e.g., claimed specific relative release rates; specific blood plasma levels recited in the claims, etc.), as discussed above. Therefore, Appellants respectfully request that §103(a) Rejection based on U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. of claims 37, 38, 44 and 45 be removed.

C. Conclusion

Appellants' claimed loratadine containing transdermal delivery systems and the use of said systems in methods of treating allergic conditions are substantially different from the formulations and methods described in Kogan et al. and Hille et al., individually or combined. The claimed transdermal delivery systems and methods have limitations which are neither taught nor suggested by either Kogan et al. and/or Hille et al. Appellants believe that, for the foregoing reasons, the final rejections of claims should be reversed.

Prompt consideration of the arguments presented herein and reversal of the final rejections is earnestly solicited.

Respectfully submitted,
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X. CLAIMS APPENDIX

LISTING OF CLAIMS

Claims 1-7. (Cancelled)

Claim 8. (Previously Presented) A method of effectively treating seasonal allergic rhinitus, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state from about 1 to about 3 ng/ml;

said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 9. (Original) The method of claim 8 wherein the plasma level of loratadine at 48 hours does not decrease by more than 30% over the next 72 hours.

Claim 10. (Original) The method of claim 8, further comprising maintaining an effective mean relative release rate of said transdermal delivery system to provide a substantially first order plasma level increase of loratadine from the initiation of the dosing interval

until about 48 to about 72 hours after the initiation of the dosing interval; and thereafter providing an effective mean relative release rate to provide a substantially zero order plasma level fluctuation of loratadine until the end of at least the five-day dosing interval.

Claim 11. (Original) The method of claim 8, further comprising providing a mean relative release rate of loratadine from said transdermal delivery system to provide a plasma level of loratadine of at least about 0.1 ng/ml within about 6 hours after application of said transdermal delivery system onto the skin of the patient.

Claim 12. (Cancelled)

Claim 13. (Original) The method of claim 8, wherein said therapeutic plasma level is maintained from about 0.1 ng/ml to about 3.3 ng/ml during the dosing interval for said transdermal delivery system.

Claim 14. (Original) The method of claim 8, wherein said transdermal delivery system has a mean relative release rate from about 1.0 $\mu g/hour/cm^2$ to about 30.0 $\mu g/hour/cm^2$.

Claim 15. (Cancelled)

Claim 16. (Original) The method of claim 8, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours; and from about 162 $\mu g/cm^2$ to about 955 $\mu g/cm^2$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claims 17-19 (Cancelled)

Claim 20. (Previously Presented) A transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof which provides a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours; and

from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell having a receptor chamber containing a 40:60 mixture of ethanol:water; said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within 36 hours from the initiation of the dosing interval, and a plasma level of loratadine of at least about 0.1 ng/ml by about 6 hours after application of said transdermal delivery system onto the skin of a human patient; said transdermal delivery system maintaining a therapeutic blood level until the end of at least a five-day dosing interval and a plasma level of loratadine at steady-state from about 1 to about 3 ng/ml.

Claim 21. (Cancelled)

Claim 22. (Original) The transdermal delivery system of claim 20, which provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours, as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 23. (Original) The transdermal delivery system of claim 20, comprising a backing layer which is impermeable to the active substance, a pressure-sensitive adhesive reservoir layer, and optionally a removable protective layer, the reservoir layer by weight comprising 20 to 90% of a polymeric matrix, 0.1 to 30% of a softening agent, 0.1 to 20% of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% of a solvent for the loratadine or salt thereof.

Claim 24. (Original) The transdermal delivery system of claim 20, which is a laminated composite comprising (a) a polymer backing layer that is substantially impermeable to loratadine or the pharmaceutically acceptable salt thereof; and (b) a reservoir layer comprising an acrylate or silicone based pressure-sensitive adhesive, 0.1 to 20% of loratadine base or of a pharmaceutically acceptable salt thereof, 0.1 to 30% of an ester of a carboxylic acid acting as a softening agent and 0.1 to 30% of a solvent for loratadine having at least one acidic group.

Claims 25-28. (Cancelled)

Claim 29. (Previously Presented) The transdermal delivery system of claim 20, wherein said therapeutic plasma level is maintained from about 0.1 ng/ml to about 3.3 ng/ml during the dosing interval for said transdermal delivery system.

Claim 30. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system has a mean relative release rate from about 1.0 $\mu g/hour/cm^2$ to about 30.0 $\mu g/hour/cm^2$.

Claim 31. (Cancelled)

Claim 32. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours; and from about 162 $\mu g/cm^2$ to about 955 $\mu g/cm^2$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 33. (Original) The transdermal delivery system according to claim 23, wherein the backing layer is composed of a flexible material.

Claim 34. (Original) The transdermal delivery system according to claim 23, wherein the backing layer is selected from the group consisting of a flexible material, an inflexible material, and an aluminum foil.

Claim 35. (Previously Presented) The transdermal delivery system according to claim 23, wherein the polymeric matrix is at least one of rubber, a synthetic homo-, co- or blockpolymer, a urethane and silicone.

Claim 36. (Original) The transdermal delivery system according to claim 23, wherein the softening agent is at least one of dodecanol, undecanol, octanol, a glycol and glycanol.

Claim 37. (Original) The transdermal delivery system according to claim 23, wherein the solvent is a monoester of a dicarboxylic acid.

Claim 38. (Original) The transdermal delivery system according to claim 23, wherein the solvent is at least one of monomethyl glutarate and monomethyl adipate.

Claim 39. (Cancelled)

Claim 40. (Original) The transdermal delivery system according to claim 23, wherein by weight the polymer is present in about 55%, the loratadine in about 10%, the solvent in about 10% and the softener in about 15%.

Claim 41. (Original) A transdermal delivery system according to claim 23, wherein the solvent is present in from about 25 to 100% the weight of the loratadine.

Claim 42. (Original) The transdermal delivery system according to claim 23, which also comprises a removable protective layer.

Claim 43. (Original) The transdermal delivery system according to claim 23, wherein the pressure-sensitive adhesive reservoir layer comprises a polymer based on an acrylate, a methacrylate, a silicone compound or a combination thereof.

Claim 44. (Previously Presented) The transdermal delivery system according to claim 23, wherein the softening agent is a medium-chain triglyceride of the caprylic/capric acids of coconut oil.

Claim 45. (Original) The transdermal delivery system according to claim 23, wherein the solvent has at least one acidic group.

Claim 46. (Previously presented) A method of effectively treating seasonal allergic rhinitus, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state from about 1 to about 3 ng/ml;

said transdermal delivery device comprising a backing layer which is substantially impermeable to the loratadine or pharmaceutically acceptable salt thereof; and a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof;

said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin , said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 47. (Previously Presented) The method of claim 8, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 $\mu g/cm^2/hr$ to about 8.5 $\mu g/cm^2/hr$ at 120 hours;

from about 2.4 $\mu g/cm^2/hr$ to about 7.7 $\mu g/cm^2/hr$ at 144 hours;

and from about 1.5 $\mu g/cm^2/hr$ to about 6.7 $\mu g/cm^2/hr$ at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 48. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 $\mu g/cm^2/hr$ to about 8.5 $\mu g/cm^2/hr$ at 120 hours;

from about 2.4 $\mu g/cm^2/hr$ to about 7.7 $\mu g/cm^2/hr$ at 144 hours;

and from about 1.5 $\mu g/cm^2/hr$ to about 6.7 $\mu g/cm^2/hr$ at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 49. (Previously Presented) The method of claim 46, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 $\mu g/cm^2/hr$ to about 8.5 $\mu g/cm^2/hr$ at 120 hours;

from about 2.4 $\mu g/cm^2/hr$ to about 7.7 $\mu g/cm^2/hr$ at 144 hours;

and from about 1.5 $\mu g/cm^2/hr$ to about 6.7 $\mu g/cm^2/hr$ at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a

human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

XI. RELATED PROCEEDINGS APPENDIX

-NONE-

XII. EVIDENCE APPENDIX

1. Copy of U.S. 4,910,205 to Kogan et al. attached herewith
2. Copy of U.S. 5,240,711 to Hille et al.
3. Copy of Smith Kline Diagnostics, Inc. v. Helena Laboratories Corporation, 859 F. 2d 878 (Fed. Cir. 1988).

References 1 and 2 listed above were made of record by the Examiner in the November 12, 2003 Office Action.

Reference 3 is cited on page 12 of this brief.

LEXSEE 859 F.2D 878,AT 887

SMITHKLINE DIAGNOSTICS, INC., Plaintiff-Appellant, v. HELENA LABORATORIES CORPORATION, Defendant/Cross-Appellant

Nos. 87-1532, 87-1533

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

859 F.2d 878; 1988 U.S. App. LEXIS 13995; 8 U.S.P.Q.2D (BNA) 1468

October 12, 1988, Decided

PRIOR HISTORY: [**1]

Appealed from: U.S. District Court for the Eastern District of Texas, Beaumont Division, Judge Fisher.

LexisNexis(R) Headnotes

COUNSEL:

Donald Dunner, Finnegan, Henderson, Farabow, Garrett and Dunner, of Washington, District of Columbia, argued for Plaintiff-Appellant. With him on the brief was Allen M. Sokal. Also on the brief were Alan D. Lourie and Stuart R. Suter, of Philadelphia, Pennsylvania, of Counsel.

Jerald I. Schneider, Cullen, Sloman, Cantor, Grauer, Scott & Rutherford, P.C., of Detroit, Michigan, argued for Defendant/Cross-Appellant. With him on the brief was Charles R. Rutherford.

JUDGES:

Rich, Circuit Judge, Nichols, Senior Circuit Judge, and Nies, Circuit Judge.

OPINIONBY:

NIES

OPINION:

[*879] NIES, Circuit Judge.

SmithKline Diagnostics, Inc. (SKD) appeals the final judgment of the United [*880] States District Court for the Eastern District of Texas, *SmithKline Diagnostics, Inc. v. Helena Laboratories Corp.*, 662 F. Supp. 622 (E.D. Tex. 1987), holding United States Patent No. 4,365,970 ('970) valid as between the parties but not infringed by either of two accused products of Helena Laboratories Corp. Based on its holding of noninfringement, the court [**2] dismissed SKD's complaint. SKD appeals the findings of noninfringement. In a cross appeal, Helena asserts that if the judgment of noninfringement is not affirmed, this court should reverse the judgment that the asserted claims are not invalid for obviousness. Helena also asserts error in that the court did not uphold other pleaded defenses or its counterclaim for unfair competition, matters on which the court made no explicit findings or conclusions.

We affirm the judgment of validity, but on different grounds from those stated by the district court. On the issue of infringement, we affirm the finding that Helena's product containing lead acetate does not infringe the asserted claims but reverse with respect to Helena's product containing hemoglobin. Helena has failed to persuade us that the record shows triable issues on the other matters raised in its cross appeal. Thus, we affirm-in-part on modified grounds, reverse-in-part, and remand for calculation of damages.

I

BACKGROUND

SKD owns the '970 patent, issued to two of its employees, Dr. Paul Lawrence and Charles Townsley, on December 28, 1982. The patent covers a specimen test slide and method for detecting occult (hidden [**3] or invisible) blood in fecal matter, an early symptom of a variety of gastroenterological diseases including colorectal cancer. More specifically, the test slide contains a piece of paper impregnated with a colorless compound, guaiac, which turns blue in the presence of a developing solution, such as hydrogen peroxide, and a catalyst, such as hemoglobin in the blood. Thus, a blue color indicates blood is present, a "positive" result; the absence of blue, a "negative" result, indicates the absence of blood. In practice, a patient places fecal samples on each of several designated test areas on the slide and returns the slide to his physician or a laboratory for testing. To test, a developing solution is placed on the test areas, and the areas are observed for color. This much of the subject invention is in the prior art. *See* United States Patent No. 3,996,006

(issued to Pagano on Dec. 7, 1976).

It is important to verify that the guaiac paper and developing solution are working properly. If either the paper or solution has lost effectiveness, a false negative result may occur, failing to detect the presence of existent cancer. Conversely, if the paper or solution becomes contaminated, [**4] a false positive test may occur, causing patient anxiety and unnecessary clinical investigations. To ensure accuracy, separate materials (external controls) were sold which could be used to check that the paper and solution were actually working. The parties dispute whether external controls consisted only of a representative unused slide from a batch of slides or also included a slide having three test areas with only one area being used for the fecal smear, the others for testing performance of the product. There is no dispute, however, that in either case the control was not built into the slide.

The invention of the '970 patent improves on the Pagano test slide and separate verification controls by providing built-in positive and negative monitors separate from the test areas. The positive monitor contains (i.e., is printed with) a catalyst, which must be a compound that reacts to environmental conditions in a manner similar to hemoglobin. The negative monitor lacks the catalyst; thus, it consists of the guaiac-laden paper alone. In practice, developing solution is added to the two monitors after it is applied to the fecal test areas. A blue color on the positive monitor indicates [**5] that the paper and solution are working. The absence of blue on the negative monitor assures that the slide has avoided contamination.

[*881] SKD asserts that independent device claim 1, claims 2 and 4 which depend from claim 1, and independent method claim 5 of the '970 patent are infringed. n1 Claims 1 and 5, the only independent claims asserted, both contain the limitation that the catalyst of the positive monitor is "a compound that reacts to environmental conditions in a manner similar to hemoglobin." Whether that claim limitation, as properly interpreted, excludes hemoglobin itself is critical, as we shall see, to the issues of validity and infringement.

n1 The '970 patent claims asserted to be infringed are:

> 1. In an occult blood specimen test slide having a front panel, a rear panel, said front panel having one or more openings, sheet means carrying a test reagent between the front and rear panels underlying each of said openings, a hinged cover adapted to overlie a portion of the front panel and said openings and flap means in the rear panel opposite said openings and pivotable to expose the underside of the sheet, the improvement comprising: an area positioned on a portion of the sheet means facing the rear panel and isolated from the openings in the front panel, said area including a positive and negative monitor, said positive and negative monitors including the test reagent and said positive monitor additionally including a compound that reacts to environmental conditions in a manner similar to hemoglobin.
>
> 2. The slide of claim 1 in which the compound in the positive monitor is a blood component and the test reagent is guaiac.
>
> 4. The slide of claim 2 in which the positive and negative monitors are framed by a brightly colored inert border.
>
> 5. In a method for determining the presence of occult blood in a specimen test slide having a guaiac treated specimen receiving sheet between a front panel and a rear panel with openings in the front and rear panels and pivotable covers to cover said openings which consists of smearing fecal matter onto the guaiac sheet through an opening of the front panel and applying a developing solution to the guaiac sheet at the corresponding opening in the rear panel the improvement which comprises further applying the developing solution to an area positioned on a portion of the sheet facing the rear panel and isolated from the openings in the front panel, said area including a positive and negative monitor, said positive and negative monitors including the guaiac and said positive monitor additionally including a compound that reacts to environmental conditions in a manner similar to hemoglobin.

[**6]

When the '970 patent issued in December of 1982, SKD was marketing a slide, under the trademark HEMOCCULT, which contained hemin as the catalyst.

At that time, Helena had competitive slide products on the market, sold under its COLOSCREEN mark, which used hemoglobin as the catalyst in a positive test monitor. Later, in April of 1984, Helena changed to use of lead acetate rather than hemoglobin as the positive monitor's catalyst. Until November 1985, however, Helena continued to enclose literature in its slide packages stating that the positive monitor contained hemoglobin.

SKD asserted infringement of the '970 claims, both literally and under the doctrine of equivalents, by the Helena products containing hemoglobin. With respect to Helena's lead acetate product, SKD asserted that Helena should be estopped to deny that its product contains hemoglobin because it continued to indicate that the product contained hemoglobin after the change was made to lead acetate. SKD did not assert that the lead acetate product would be covered by the claims but for the misrepresentation.

Helena contended that its products containing hemoglobin do not infringe because the claim language "similar [**7] to hemoglobin" literally excludes hemoglobin itself, and that the prosecution history precludes interpreting the claim to cover a hemoglobin product. Helena also asserted that the '970 claims in issue are invalid as obvious within the meaning of 35 U.S.C. § 103 (1982), and invalid under 35 U.S.C. § 116 (1982) for failure to name the proper inventors. In addition, Helena asserted the defense of inequitable conduct and raised an unfair competition counterclaim.

The district court interpreted the claim limitation at issue as excluding hemoglobin itself. Based upon that interpretation, the court found the invention of the '970 patent nonobvious. Had the claims covered hemoglobin, however, the court stated that the claim would have been invalid as obvious over prior art disclosing hemoglobin as a catalyst in positive test monitors.

[*882] Under its interpretation of the claim limitation "similar to hemoglobin" recited in claims 1 and 5, the court found Helena's hemoglobin-containing slides noninfringing, either literally or under the doctrine of equivalents. It rejected SKD's estoppel argument with respect to Helena's products containing [**8] lead acetate. It further held that, if Helena were found to infringe, the infringement was not willful, an issue not appealed.

Neither in its judgment nor in its findings of fact and conclusions of law did the district court mention Helena's other defenses or its counterclaim for unfair competition. Both parties have appealed, each asserting error in certain findings and conclusions made adverse to them, and each raising various arguments concerning issues not explicitly ruled on by the court.

II

OPINION

A. *Claim Interpretation*

The claims of the '970 patent measure the invention at issue; thus, the claims must be interpreted and given the same meaning for purposes of both validity and infringement analyses. *See, e.g., SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121, 227 U.S.P.Q. (BNA) 577, 585 (Fed. Cir. 1985) (in banc). To ascertain the meaning of the claims, we look to the claim language, the specification, and the prosecution history. *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576, 1579, 6 U.S.P.Q.2D (BNA) 1557, 1560 (Fed. Cir. 1988); [**9] *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 867, 228 U.S.P.Q. (BNA) 90, 93 (Fed. Cir. 1985). Also relevant are the other claims and expert testimony. *See, e.g., Perini America, Inc. v. Paper Converting Mach. Co.*, 832 F.2d 581, 584, 4 U.S.P.Q.2D (BNA) 1621, 1624 (Fed. Cir. 1987). Moreover, the claims should be construed as one skilled in the art would construe them. *Specialty Composites v. Cabot Corp.*, 845 F.2d 981, 986, 6 U.S.P.Q.2D (BNA) 1601, 1604 (Fed. Cir. 1988).

This court reviews a district court's claim interpretation as a matter of law, unbridled by the constraints of the "clearly erroneous" standard of review. That interpretation may depend, as here, however, on evidentiary material which requires resolution of factual issues, such as what occurred during the prosecution history. *See, e.g., ZMI Corp.*, 844 F.2d at 1578, 6 UPSQ2d at 1559; *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1054, 5 U.S.P.Q.2D (BNA) 1434, 1441 (Fed. Cir. 1988); *Tandon Corp. v. United States Int'l Trade Comm'n*, 831 F.2d 1017, 1021, 4 U.S.P.Q.2D (BNA) 1283, 1286 (Fed. Cir. 1987). [**10] We review resolution of those factual issues under the clearly erroneous standard. *See, e.g., Perini America*, 832 F.2d at 584, 4 USPQ2d at 1624.

The dispute in this case centers on the meaning of the claim limitation "including a compound that reacts to environmental conditions in a manner similar to hemoglobin," which appears in independent claims 1 and 5 and is, of course, a limitation in dependent claims 2 and 4. Helena argues, and the district court concluded, that the phrase must be interpreted to exclude hemoglobin itself. On the other hand, SKD contends that the phrase encompasses hemoglobin as well as other similar materials. We turn to the sources useful in claim interpretation to resolve this dispute.

1. *The Claim Language*

The first requirement in claim interpretation is to examine the claim language. *ZMI Corp.*, 844 F.2d at 1579, 6 USPQ2d at 1560; *McGill, Inc. v. John Zink Co.*, 736

F.2d 666, 672, 221 U.S.P.Q. (BNA) 944, 948 (Fed. Cir.), *cert. denied*, 469 U.S. 1037, 83 L. Ed. 2d 404, 105 S. Ct. 514 (1984). [**11] Helena argues that the "ordinary" meaning of "similar to" excludes "identical." Although that argument has a superficial logic, we cannot agree, in the context of these claims, that the phrase "similar to hemoglobin" necessarily excludes hemoglobin.

In finding that the claims exclude hemoglobin, the district court relied upon the statement of one co-inventor, Dr. Lawrence. In a report on his work, Dr. Lawrence had written that "the stabilities of the proteins [such as hemoglobin] are too short to be compatible with standard dating [*883] of HEMOCCULT slides." n2 The district court took that statement to indicate Dr. Lawrence's belief that hemoglobin would not work. 662 F. Supp. at 628.

> n2 Record of Invention, SKD, Case No. 14084, at 1 (March 12, 1981). By "instability," Dr. Lawrence referred to the tendency of catalytic compounds to decay over time.

Taken in context, however, Dr. Lawrence's statement does not indicate that he believed hemoglobin would not work at all, as shown in the [**12] following additional excerpts from the report:

> A variety of catalysts may be printed: for example, . . . Fe/protopurphyrin (hemin); homo proteins such as hemoglobin (Hb) . . . may be similarly used.
> Printing of proteins such as Hb . . . presents practical difficulties. High concentrations are required. . . . More important, once printed the stabilities of the proteins are too short to be compatible with standard [three year] dating of Hemoccult(R) slides. . . .
> . . . .
> Hemin spots have a dated stability comparable or greater than Hemoccult(R) slides.

Nowhere does Dr. Lawrence state that hemoglobin *cannot* be used. The thrust of his analysis is a justification for his preference for hemin over other alternatives, inasmuch as it had sufficient stability to meet the standard three-year dating period. In fact, Dr. Lawrence states that hemin and hemoglobin "may be similarly used." Moreover, he testified at trial that hemoglobin would work and that methods were known for stabilizing hemoglobin, one of the problems he noted as a reason why hemin works better. In any event, the claim does not contain a limitation with respect to the duration of the catalyst's [**13] effectiveness.

We cannot conclude that the claim language indicates what characteristics the catalyst must have. The limitation at issue does not identify specific catalysts to be included or excluded. Viewed in this manner, the limitation does not exclude hemoglobin; rather, it reflects the fact that a compound similar to hemoglobin may work better than hemoglobin itself.

2. *Specification*

The limitation need not be given a more restrictive meaning in the claims of the '970 patent by reason of the specification. The specification of the '970 patent shows a clear intent by the inventors to include hemoglobin when they claimed their invention. It states:

> Since guaiac-based fecal occult blood tests are actually testing for the catalytic activity of hemoglobin in blood, the *positive monitor should employ either hemoglobin or a catalyst which would react to adverse environmental conditions in a manner similar to hemoglobin. Preferably*, the test slide of this invention employs *hemin*, a hemoglobin derived catalyst, as the catalyst in the positive monitor.

'970 Patent Specification, col. 4, ln. 1-8 (issued Dec. 28, 1982) (emphasis added). Thus, the specification [**14] specifically discloses hemoglobin and hemin, with the latter preferred, as compounds to be used in the positive monitor. We agree with SKD that it would be a strained interpretation to exclude hemoglobin from the claims when the specification specifically discloses it as a viable candidate for the positive monitor catalyst.

Helena offers a convoluted argument to overcome the specification's disclosure of hemoglobin as a catalyst. The argument begins with the premise that the '970 patent describes two functions for the monitor: testing both for proper functioning of the chemicals (guaiac and developer) and for deterioration of the fecal sample caused by the environment. (Other suppliers' slides test only the former and use hemoglobin). Thus, Helena asserts, the patent requires a control that deteriorates in the same way as the blood deteriorates in the fecal sample. Hemoglobin does not deteriorate like blood (note the instability problem Dr. Lawrence related), hence, Helena reasons, the patent claims cannot include hemoglobin. Per Helena, the specification suggests instead that hemin will perform both functions in the positive monitor, as [*884] will a compound that "reacts [**15] to environmental conditions in a manner similar to hemoglobin" in the blood of the fecal sample.

Helena's argument fails for a number of reasons. Most

basic is the fact that neither the claims nor the specification require the positive monitor catalyst to deteriorate like blood in a fecal sample. In addition, the argument ignores entirely the specific disclosure in the specification that hemoglobin is a suitable compound for use as the catalyst. Finally, Helena offers no evidence to show that hemin, which it argues is encompassed by the claims, is relatively more like blood in the fecal samples in terms of deterioration than is hemoglobin.

3. *Prosecution History*

The prosecution history is still another tool useful for claim interpretation. *See, e.g., ZMI Corp.*, 844 F.2d at 1580, 6 USPQ2d at 1561; *McGill Inc.*, 736 F.2d at 673, 221 USPQ at 949. The district court relied most heavily on that tool and determined that, through a claim amendment, the inventors had narrowed the claims to exclude hemoglobin.

The claim limitation at issue was not present in the original claims as filed with the United States Patent and Trademark Office (PTO). [**16] Instead, claim 1 provided "the improvement comprising: a control area having a positive and a negative monitor said control area positioned on a portion of the sheet." The Examiner rejected the claims as obvious under 35 U.S.C. § 103 (1982), citing United States patents to Pagano (3,996,006) and Friend (4,175,923).

Friend discloses a "throw-in-the-bowl" type of test product made of paper impregnated with guaiac. A section of the paper also has impregnated a blood component (forming a built-in positive monitor). The user sprays the entire paper sheet with developer and first observes it to confirm that the guaiac chemical is working properly. Proper functioning is assured if the part of the paper impregnated with blood component turns blue. The user then drops the product into a toilet bowl containing fecal matter, where the remainder of the paper will turn blue if the fecal matter contains blood or will remain white, indicating the absence of blood.

The Examiner maintained that it would have been obvious from the teaching of Friend to provide positive and negative monitors on the Pagano slide. In response to the First Office Action, on January 25, 1982, the [**17] inventors argued that "Friend fails to disclose any negative monitor or control." Thereafter, the Examiner issued a Final Action rejecting the claims as obvious: "Even though Friend is concerned with positive control, it would be obvious to the routineer that both positive and negative controls could be incorporated in Pagano."

The Examiner granted the inventors an interview on July 8, 1982, which the Examiner summarized as discussing the arguments "that areas are not only control but monitors of performance for both false positives and negatives" and "that prior art does not show a negative monitor that indicates false positives." The inventors described the interview, in an Amendment After Final Rejection filed on July 20, 1982, as emphasizing "that Friend fails to disclose any negative monitor or control. . . . The criticality of having a negative monitor present on the occult blood slide was thoroughly discussed at the interview." At this point in the prosecution, neither the Examiner nor the inventors had mentioned the limitation now at issue.

Those parties then conducted a telephone interview on July 27, 1982. In his Summary Record of the conversation, the Examiner states: [**18]

> Agreed to amendment of the claims as per Examiner's Amendment (Paper No. 9) to particularly recite the positive and negative monitors.

Paper No. 9 contained the amendment introducing the "similar to hemoglobin" limitation at issue. Following that amendment, the '970 patent claims were allowed on August 6, 1982.

The district court concluded that the Examiner allowed the patent claims only because of the amendment to overcome the disclosure in the Friend patent. Finding [*885] that Friend discloses use of hemoglobin as the positive monitor catalyst, the court determined that the amendment narrowed the claims to avoid that disclosure by excluding hemoglobin from the '970 claims.

Where the district court clearly erred is in its last finding, that the amendment was made to overcome the disclosed use of *hemoglobin* in a monitor. Friend does not specifically disclose or claim a hemoglobin catalyst. Rather, Friend claims "blood" as a substrate or composition for the positive monitor catalyst. Friend's patent specification discloses "commercially available dried human or animal blood" and "components of blood" as the positive catalyst. Consequently, Friend's [**19] teaching, although it includes hemoglobin as the catalyst, was not so restricted and an amendment excluding hemoglobin but including hemin (another blood component) would not have overcome Friend's broad disclosure of blood component catalysts.

Thus, we are unpersuaded that the amendment to claim subject matter "similar to" hemoglobin was made to overcome Friend's disclosure of a hemoglobin catalyst. The purpose of the amendment is unclear. SKD reads the Examiner's statement that the amendment was made "to particularly recite the positive and negative monitors" lit-

erally and contends that the amendment was made only to satisfy the definiteness requirement of 35 U.S.C. § 112 (1982) ("The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."), and not to avoid an obviousness rejection based upon the prior art. We need not determine the purpose for the amendment. We merely hold that the district court's finding, that the amendment was made to overcome Friend's disclosure of a hemoglobin catalyst, is clearly erroneous.

4. *Conclusion*

The district [**20] court's findings that the inventor believed hemoglobin would not work and that the claims were amended to exclude hemoglobin disclosed as a catalyst in the prior art are clearly erroneous. We conclude, as a matter of law, that the asserted claims of the '970 patent, properly interpreted, include hemoglobin itself, as well as compounds that react to environmental conditions in a manner similar to hemoglobin, as a positive monitor catalyst.

Because we have determined that the district court improperly interpreted the claims, the remainder of its decisional process on the issues of validity and infringement is distorted. *See, e.g., Panduit Corp.*, 810 F.2d 1561, 1576, 1 U.S.P.Q.2D (BNA) 1593, 1603 (Fed. Cir.) ("When the prior art is compared with erroneously interpreted claims, findings of differences between the prior art and the claims will necessarily be clearly erroneous."), *cert. denied*, 481 U.S. 1052, 107 S. Ct. 2187, 95 L. Ed. 2d 843 (1987); *Moeller v. Ionetics, Inc.*, 794 F.2d 653, 656, 229 U.S.P.Q. (BNA) 992, 994 (Fed. Cir. 1986) [**21] (improper claim construction can distort entire infringement analysis). Keeping this in mind, we now turn to those issues.

B. *Validity*

1. *Obviousness*

a. *The Standard*

Helena challenges validity of the '970 patent on the grounds that the claimed invention would have been obvious within the meaning of 35 U.S.C. § 103 (1982). n3 In evaluating that challenge, the district court properly began its analysis with the presumption that the patent is valid. *See* 35 U.S.C. § 282 (1982). That presumption places the burden of proof of facts, and the ultimate burden of persuasion to establish invalidity, on Helena. *See, e.g., Carella v. Starlight Archery & Pro Line Co.*, 804 F.2d 135, 138, 231 U.S.P.Q. (BNA) 644, 646 (Fed. Cir.), *amended* 1 U.S.P.Q.2D (BNA) 1209 [*886] (Fed. Cir. 1986). In reviewing the district court's factual findings underlying its conclusion, we are governed by the clearly erroneous standard. *See, e.g., Panduit Corp.*, 810 F.2d at 1566, 1 USPQ2d at 1595-96. [**22] We review the conclusion of obviousness or nonobviousness drawn from the facts so reviewed as a matter of law. *Id.* at 1569, 1 USPQ2d at 1598.

n3 Section 103 provides in relevant part:

> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

b. *The Factual Inquiries*

Although the district court upheld the validity of the claims in issue, it did so only if the claims were interpreted to exclude hemoglobin. 662 F. Supp. at 626. Having concluded that hemoglobin is within the claims, we can affirm the judgment of validity only if the facts are undisputed or if the court made other findings which lead to that same legal [**23] conclusion of nonobviousness despite the claims' coverage of hemoglobin. n4 The latter situation occurs here. The court found that "the '970 patent discloses and claims the *first* fecal occult blood specimen test *slides having built-in positive and negative monitors* for verifying the proper performance of the slide." *Id.* at 624 (emphasis added). The court also made the following findings which are pertinent to the issue of nonobviousness:

> Dr. Lawrence of SKD, a coinventor of the '970 patent, followed a different approach [from that historically taken], namely a [sic] built-in positive and negative controls on each slide. This had the advantage of verifying the performance of every slide and it was much easier to use than external controls. Furthermore, a built-in positive monitor printed during manufacturing gave more reproducible results than external controls that were applied in variable amounts. Dr. Lawrence's approach was also new in that he no longer sought only controls that simulated feces. Monitors that indicated only whether the slide and developer were working properly avoided the confusion that could result from comparing the test results [**24] on the

actual fecal specimen and on the monitors.

Id. at 625.

n4 An appellate court may make a finding of fact on evidence that is undisputed. *See, e.g., King v. Commissioner of Internal Revenue*, 458 F.2d 245, 249 (6th Cir. 1972); *Sbicca-Del Mac, Inc. v. Milius Shoe Co.*, 145 F.2d 389, 400, 63 U.S.P.Q. (BNA) 249, 260 (8th Cir. 1944); 9 C. Wright & A. Miller, *Federal Practice & Procedure: Civil* § 2577 at 699-701 (1971) ("It is settled that findings are not jurisdictional and the appellate court may decide the appeal without further findings if it feels that it is in a position to do so. . . . A remand has been thought unnecessary if all the evidence is documentary or if the facts are undisputed.") (footnotes omitted); *cf. B.D. Click Co. v. United States*, 222 Ct. Cl. 290, 614 F.2d 748, 755 (1980). An appellate court may also make such a finding even when the evidence is disputed if, as a matter of law, the court could only make one finding of fact or decide the fact in only one way. Otherwise, protracted litigation and unnecessary delay and expense would occur. *B.D. Click*, 614 F.2d at 755.

[**25]

The above analysis would lead to a conclusion of nonobviousness even if hemoglobin is the catalyst. The court did not explain why hemoglobin as the positive monitor catalyst changed that analysis, and we see none. Helena maintains that the court erred in not holding the claims invalid, whether or not hemoglobin is the catalyst, because the improvement of placing monitors on a Pagano slide is obvious from the Friend teaching of a positive monitor on the throw-in-the-bowl type of occult blood testing device and method. Given the nature of the Friend product, we cannot agree that the disclosure of a control in Friend (whether positive alone or positive and negative) is a sufficient teaching to make the claimed combination obvious.

Friend explicitly discloses only a positive monitor. Although never mentioned by Friend, if the portions of the paper not impregnated with blood component do not remain white when developer is applied, then product contamination would be indicated. The parties dispute whether that fact amounts to an inherent disclosure of a negative monitor. The asserted "inherent" monitor of Friend's claimed product is the test area itself, however, whereas the claims at [**26] issue require control areas which are "isolated from" the test areas on the "rear" of the slide. Merely pointing to a negative monitor in the prior art, which constitutes Helena's main argument to establish obviousness, is unpersuasive. Helena [*887] cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention. *See, e.g., Akzo N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1481, 1 U.S.P.Q.2D (BNA) 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909, 107 S. Ct. 2490, 96 L. Ed. 2d 382 (1987). Helena has the burden to show some teaching or suggestion in the references to support their use in the particular claimed combination. *Uniroyal Inc.*, 837 F.2d at 1051, 5 USPQ2d at 1438-39. A holding that combination claims are invalid based merely upon finding similar elements in separate prior art patents would be "contrary to statute and would defeat the congressional purpose in enacting Title 35." *Panduit Corp.*, 810 F.2d at 1577, 1 USPQ2d at 1605.

Friend's [**27] suggestion begins and ends with the disclosure of a built-in control. Nothing in Friend suggests the particular structure or method of the claims, read as a whole. *Id.* (claims, entire prior art, and prior art patents must each be read "as a whole"). The claimed structure positions the monitors on each slide in such a way that the fecal material may contact the slide without contaminating the control areas. *See* '970 Patent Specification at col. 2, ln. 10-18 ("These [monitors] comprise two small areas or spots printed on an isolated area of the guaiac test paper at some distance from the portions of the test paper underlying each of the [two test areas]. In this manner the positive spot (monitor) is of such shape and size and placed in such a positive relation to the stool sample(s) that there can be no confusion of its blue color with that of a positive stool sample."). This location provides the advantage that the fecal matter may be conveniently tested at a later time by a laboratory or physician, at which time the monitors will also be activated. *See id.* at col. 3, ln. 38-53 ("To use the slide, the patient . . . applies with an applicator a thin smear of specimen [**28] from a portion of his stool on sheet 32 through opening 30. . . . The cover is then closed. . . . The patient returns the slide either to his physician or a laboratory. The physician or technician [adds] developing solution . . . [and] the test results are then observed.").

Helena also asserts that the claim language is so broad that it would encompass prior art controls in which a blood component for monitoring purposes is not originally on the slide. On the other hand, SKD asserts that the claims require that the monitor must be built into the slide. We agree with SKD.

The specification states that:

It is still a further object of this invention to provide a simple, rapid, convenient, inexpen-

> sive and *built-in control test* which would monitor the test reagents from the date of manufacture to the date of development.

Id. at col. 2, ln. 2-6 (emphasis added). That portion of the specification supports the district court's view that "the '970 patent discloses and claims the first fecal occult blood specimen test slide having built-in positive and negative monitors for verifying the proper performance of the slide." 662 F. Supp. at 624. [**29] The claims that the district court was referring to when it stated its view were claims 1 and 5, which require "an area *positioned on* a portion of *the sheet* . . ., said area including a positive and negative monitor." (Emphasis added.) Thus, we agree with the district court's interpretation that the '970 patent claims a test slide having built-in positive and negative monitors. Accordingly, we conclude that, fairly read, the claims cover only slides in which the catalyst is built into the slide itself.

We also agree with the district court that some, but not overwhelming, support for a conclusion of nonobviousness is provided by the objective evidence. *See, e.g., W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1555, 220 U.S.P.Q. (BNA) 303, 314 (Fed. Cir. 1983) (Objective evidence of nonobviousness "may in a given case be entitled to more weight or less, depending on its nature and its relationship to the merits of the invention. It may be the most pertinent, probative, and revealing evidence available" on the issue.), *cert. denied*, 469 [*888] U.S. 851, 105 S. Ct. 172, 83 L. Ed. 2d 107 (1984). n5

> n5 We need not decide whether, had resolution of the factual inquiries presented a "clear and very strong case of obviousness," *EWP Corp. v. Reliance Universal Inc.*, 755 F.2d 898, 907, 225 U.S.P.Q. (BNA) 20, 25 (Fed. Cir.), *cert. denied*, 474 U.S. 843, 88 L. Ed. 2d 108, 106 S. Ct. 131 (1985), rather than nonobviousness, the objective evidence provided would have outbalanced that case and shown nonobviousness.

[**30]

c. *Conclusion*

After consideration of all of Helena's arguments, we are unpersuaded that the facts established by the record lead to the conclusion that the claims of the '970 patent are invalid under 35 U.S.C. § 103. Accordingly, we affirm the district court's judgment of validity, but on different grounds from those stated by that court.

2. *Inventorship*

Helena contends that the '970 patent is invalid because it does not satisfy the requirement that the true inventor or inventors be named. n6 The springboard to that contention is Helena's interpretation of the '970 patent claims as not restricted to built-in control monitors. Using that springboard, Helena asserts that the patent claims match the work done by Lawrence's and Townsley's predecessors at SKD. We agree with the district court, however, that the claims are restricted to built-in monitors. Helena does not contend that Lawrence and Townsley were not the true inventors of the claimed subject matter when the claims are so interpreted.

> n6 The patent statute provides that "whoever invents or discovers" the patentable subject matter "may obtain a patent therefor." 35 U.S.C. § 101 (1982).

[**31]

Helena frames an additional challenge to the '970 patent on the grounds that the named joint inventors did not jointly invent every claim in the '970 patent. SKD does not contest that fact; instead, it relies on the current patent statute, which provides:

> Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.

35 U.S.C. § 116 (1982) (as amended by the Patent Law Amendments Act of 1984, Pub. L. No. 98-622, 98 Stat. 3383 (1984) (hereinafter, "the Act")). If this section applies to the '970 patent, Helena's challenge fails. We hold that section 116 applies.

The 1984 amendments made a number of substantive changes in the patent statute. Section 106(a) of the Act, *reprinted at* 35 U.S.C. § 103 note (Supp. II 1984), states that with certain exceptions "the amendments made by this Act . . . shall apply to all [**32] United States patents granted before, on, or after the date of enactment [Nov. 8, 1984]." At least, *prima facie*, the 1984 amendment of section 116 applies to the '970 patent. Helena asserts, however, that it does not apply retroactively because of the exception provided in section 106(e). Section 106(e) states: "The amendments made by this Act shall not affect the right of any party in any case pending in court on the date of enactment to have their rights determined on the

basis of the substantive law in effect prior to the date of enactment." This case was pending on November 8, 1984, the date of enactment. The "substantive law" in effect on that date, per Helena, was that a patent was invalid for failure to name proper inventors unless the inventorship entity named was the true origin of *every* claim in a patent containing more than one claim, i.e., the "all claims" rule.

Helena's argument fails because the "all claims" rule was not uniformly accepted as "the substantive law" before the 1984 Act. *Compare In re Sarett*, 51 C.C.P.A. 1180, 327 F.2d 1005, 1010 n.7, 140 U.S.P.Q. (BNA) 474, 479 n.7 (CCPA 1964); *In re Hamilton*, 17 C.C.P.A. 833, 37 F.2d 758, 759, 4 USPQ 224, 227 (CCPA 1930); [**33] *Rival Mfg. Co. v. Dazey Prods. Co.*, 358 F. Supp. 91, 101, 177 U.S.P.Q. (BNA) 432, 439 (W.D. Mo. 1973); *Stewart v. Tenk*, 32 F. 665, 666 (S.D. Ill. 1887), *with United States v. Telectronics, Inc.*, 658 F. Supp. 579, 592, 3 U.S.P.Q.2D (BNA) 1571, 1580 (D. Colo. 1987); *Vekamaf Holland B.V. v. Pepe* [*889] *Benders, Inc.*, 211 UPSQ 955, 966-67 (D. Minn. 1981); *SAB Industri AB v. Bendix Corp.*, 199 U.S.P.Q. (BNA) 95, 104 (E.D. Va. 1978). The 1984 amendment clearly repudiates the rule. *See generally* 1 D. Chisum, *Patents*, § 2.03[3] at 2-25 to-28 (1987).

We do not believe Congress intended, by the exception of section 106(e), to give a litigant a right to invoke the law of a particular circuit on joint inventorship or to preserve a conflict, even for a limited time, between circuits on this issue. Thus, we hold that section 106(e) does not negate the applicability of amended section 116 to the '970 patent and Helena's challenge fails.

C. *Infringement*

1. *Literal Infringement*

This court has repeatedly stated that [**34] direct infringement requires a two-step analysis. The claimed invention must first be defined, a legal question of claim interpretation. Second, the trier of fact must determine whether the claims, as properly interpreted, cover the accused device or process. The second step involves a question of fact. *See, e.g., Specialty Composites*, 845 F.2d at 986, 6 USPQ2d at 1603; *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 758, 221 U.S.P.Q. (BNA) 473, 477 (Fed. Cir. 1984); *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1569, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983). The burden is on SKD, as the patent owner, to prove infringement by a preponderance of the evidence. *See, e.g., Uniroyal, Inc.*, 837 F.2d at 1054, 5 USPQ2d at 1441. Such proof must show that every limitation of the patent claims asserted to be infringed is found in the accused device, either literally or by an equivalent. *See Pennwalt Corp. v. Durand-Wayland, Inc.*, 833 F.2d 931, 935, 4 U.S.P.Q.2D (BNA) 1737, 1739-40 (Fed. Cir. 1987) (in banc), *cert. denied*, 485 U.S. 961, 108 S. Ct. 1226, 99 L. Ed. 2d 426 (1988), 485 U.S. 1009, 108 S. Ct. 1474, 99 L. Ed 2d 703 (1988). [**35]

We have already performed the first step of the analysis above and have determined that, properly interpreted, independent claims 1 and 5 cover hemoglobin as the positive monitor catalyst. n7 Based upon that interpretation, the second step of the analysis follows without extended commentary. There is no dispute that, before Helena changed its catalyst to lead acetate, Helena's slides contained hemoglobin as the positive monitor catalyst. Moreover, Helena does not contend that its accused product does not embody every other limitation of the asserted claims. Accordingly, any finding other than that the '970 patent claims literally read on Helena's slides containing hemoglobin would be clearly erroneous.

> n7 Having construed the claims one way for determining validity, it is axiomatic that the claims must be construed in the same way for infringement. *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 842 F.2d 1275, 1279, 6 U.S.P.Q.2D (BNA) 1277, 1280 (Fed. Cir. 1988); *Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1449, 223 U.S.P.Q. (BNA) 603, 610 (Fed. Cir. 1984); *cf. Autogiro Co. of Am. v. United States*, 181 Ct. Cl. 55, 384 F.2d 391, 399, 155 U.S.P.Q. (BNA) 697, 704, (1967) (patentee cannot construe claims narrowly before Patent Office and later broadly before court).

[**36]

2. *Reverse Doctrine of Equivalents*

A finding that the words of the claims literally read on the accused device does not necessarily end the infringement inquiry. Although SKD has carried its burden and proven that the '970 patent claims asserted read on Helena's hemoglobin-containing slides, Helena may establish the fact of noninfringement by carrying its burden of going forward to show its device "has been so far changed in principle that it performs the same or similar function in a substantially different way." *SRI Int'l*, 775 F.2d at 1123-24, 227 USPQ at 587; *see also Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608-09, 94 L. Ed. 1097, 70 S. Ct. 854 (1950). Helena has attempted to carry its burden by pointing to Dr. Lawrence's alleged admission that hemoglobin would not work. Helena's argument, which the district court accepted, 662 F. Supp. at 628, is that Dr. Lawrence's statement indicates hemoglobin operates in a substantially different way from the compounds SKD successfully used as positive monitor catalysts. [**37]

[*890] As indicated above, Dr. Lawrence never stated that hemoglobin would not work as a catalyst. Claims 1 and 5 of the '970 patent cover compounds that react to environmental conditions in a manner similar to hemoglobin. We have held these claims to include hemoglobin itself as one possible catalyst. Thus, hemoglobin does not operate in a substantially different way from the compounds claimed—which include hemoglobin—and we reject Helena's argument based on the reverse doctrine of equivalents. n8

> n8 Because we have decided that Helena's accused product containing hemoglobin as the positive monitor catalyst literally infringes the '970 patent claims, we need not and do not review the district court's analysis of infringement under the doctrine of equivalents.

3. *Estoppel to Deny Infringement*

With respect to Helena's slides containing lead acetate as the catalyst in the positive monitor, SKD concedes those slides do not infringe the '970 patent either literally or under the doctrine of [**38] equivalents. SKD poses, however, a unique "infringement by estoppel" theory. In April 1984, Helena began marketing COLOSCREEN slides containing lead acetate in place of hemoglobin, but failed to alter a package insert stating that the positive monitor contained hemoglobin. The insert was not corrected until November 1985. SKD's theory is that Helena, by incorrectly identifying hemoglobin as the catalyst in the positive monitor, obtained sales to customers who would not otherwise have purchased Helena's product. Had customers known Helena's product did not contain a catalyst similar to the hemoglobin the test was designed to discover, SKD argues, they would not have purchased Helena's product. Having obtained the benefit of such sales, Helena should be estopped, per SKD, from denying that the COLOSCREEN slides marketed between April 1984 and November 1985 contain hemoglobin. Accordingly, because slides containing hemoglobin infringe the '970 patent, the lead acetate slides, per SKD, infringe by estoppel.

The district court rejected SKD's position that these facts establish an estoppel. SKD's theory of estoppel rests on *Crane Co. v. Aeroquip Corp.*, 364 F. Supp. 547, 179 U.S.P.Q. (BNA) 596 (N.D. Ill. 1973), [**39] *aff'd in part & rev'd in part on other grounds*, 504 F.2d 1086, 183 U.S.P.Q. (BNA) 577 (7th Cir. 1974), and its assertion that the case is "completely analogous and should be followed in this case." In *Crane*, Crane licensed Aeroquip to manufacture pipe couplings under the former's patent. Aeroquip then modified its product, which the district court found did not infringe Crane's patent, but continued to place Crane's patent number on its modified couplings. Citing "marking estoppel" cases, n9 the district court found Aeroquip "estopped to deny that it is *liable for royalties* on [the modified] couplings." 364 F. Supp. at 560, 179 USPQ at 606-07 (emphasis added). The Seventh Circuit found that the modified couplings came within the scope of the claims and, thus, expressed "no opinion" on the marking estoppel issue. 504 F.2d at 1093, 183 USPQ at 581.

> n9 We note the line of cases sometimes called "marking estoppel" cases, in which, under some circumstances, a party that marks its product with a patent number is estopped from asserting that the product is not covered by the patent. *See, e.g., Gridiron Steel Co. v. Jones & Laughlin Steel Corp.*, 361 F.2d 791, 796-97, 149 U.S.P.Q. (BNA) 877, 880-81 (6th Cir. 1966); *Collis Co. v. Consolidated Mach. Tool Corp.*, 41 F.2d 641, 645, 6 USPQ 109, 113 (8th Cir.), *cert. denied*, 282 U.S. 886, 51 S. Ct. 90, 75 L. Ed. 781 (1930); *Piaget Novelty Co. v. Headley*, 108 F. 870, 872 (2d Cir. 1901).

[**40]

Whatever the validity of the "marking estoppel" line of cases, we do not find *Crane* applicable to the present case. Helena never took a license under SKD's patent. Accordingly, *liability for royalty* payments is not at issue here. Helena did not place an erroneous patent number on its lead acetate product; it erroneously identified the catalyst used on its product. The district court in *Crane* reached its result, in part, on the reasoning that

> it should be recognized that application of the marking estoppel doctrine in this case should have an important therapeutic function in protecting the public interest. Manufacturers should be on notice [*891] that care must be taken in avoiding misrepresentation to the public that goods are protected by a patent.

364 F. Supp. at 560, 179 USPQ at 607. Such reasoning is inapplicable to this case.

35 U.S.C. § 271(a) provides:

> Except as otherwise provided in this title, whoever without authority makes, uses or sells any patented invention, within the United States during [**41] the term of the patent therefore, infringes the patent.

Helena's lead acetate product is not the "patented invention" and, therefore, is not an infringement as defined by the statute. We do not accept the proposition that an *admittedly noninfringing* product can be converted by estoppel to an infringing product.

4. *Summary of Infringement Analysis*

Based on properly interpreted claims, Helena's slides which contain hemoglobin literally infringe the asserted claims of the '970 patent. The district court's finding of noninfringement is clearly erroneous, based as it is upon a legally erroneous interpretation of the asserted claims. We reverse that portion of the court's judgment finding noninfringement by Helena's hemoglobin-containing slides. With respect to Helena's slides containing lead acetate as the positive monitor catalyst, however, we agree with the court that SKD failed to carry its burden of proving infringement. Accordingly, we affirm the court's finding of noninfringement as to the lead acetate product.

D. *Inequitable Conduct*

In its cross appeal, Helena contends that the district court erred in failing to hold the '970 patent unenforceable. [**42] The grounds for Helena's charge of unenforceability are four alleged breaches of the duty to disclose material information, and to disclose that information accurately, to the PTO during prosecution of the '970 patent. *See* 37 C.F.R. § 1.56 (1987). Such a breach may constitute inequitable conduct sufficient to render a patent unenforceable. *See, e.g., J.P. Stevens & Co. v. Lex Tex, Ltd.*, 747 F.2d 1553, 1559, 223 U.S.P.Q. (BNA) 1089, 1092 (Fed. Cir. 1984), *cert. denied*, 474 U.S. 822, 88 L. Ed. 2d 60, 106 S. Ct. 73 (1985); *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1362-63, 220 U.S.P.Q. (BNA) 763, 773 (Fed. Cir.), *cert. denied*, 469 U.S. 821, 83 L. Ed. 2d 41, 105 S. Ct. 95 (1984).

Having found no infringement, the district court apparently did not consider it necessary to reach the question of enforceability. Because we reverse the finding of noninfringement, the defense of inequitable conduct must be considered. [**43] When the pertinent facts are undisputed, as here, an appellate court need not remand for the trial court to make findings and conclusions but may resolve the issue. *See, e.g., Icicle Seafoods, Inc. v. Worthington*, 475 U.S. 709, 714, 89 L. Ed. 2d 739, 106 S. Ct. 1527 (1986); *UMC Elecs. Co. v. United States*, 816 F.2d 647, 657, 2 U.S.P.Q.2D (BNA) 1465, 1472 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1025, 108 S. Ct. 748, 98 L. Ed. 2d 761 (1988); *see also* 28 U.S.C. § 2106 (1982) ("any . . . court of appellate jurisdiction may . . . direct the entry of such appropriate judgment . . . as may be just under the circumstances.").

To hold that a patentee has committed inequitable conduct, this court has uniformly held that *both* materiality and intent must be proven by clear and convincing evidence. *See, e.g., FMC Corp. v. Manitowoc Co.*, 835 F.2d 1411, 1415, 5 U.S.P.Q.2D (BNA) 1112, 1115 (Fed. Cir. 1987). Thus, "to be guilty of inequitable conduct, one must have intended to act inequitably." *Id.* [**44] Proof of deliberate scheming is unnecessary; gross negligence may constitute sufficient wrongful intent to support a holding of inequitable conduct. *See Reactive Metals & Alloys Corp. v. ESM, Inc.*, 769 F.2d 1578, 1583-84, 226 U.S.P.Q. (BNA) 821, 825 (Fed. Cir. 1985).

In the present case, however, there is no evidence of actual wrongful intent or gross negligence by the patentee. Helena's complete failure to present any evidence of intent likely follows its initial misunderstanding, which it later corrected, that "under the relevant case law, intent is not [*892] material to a determination of unenforceability, since Helena is *not* alleging fraud." As stated above, this court has uniformly held evidence of intent, not only material but, a *requirement* for a holding of inequitable conduct. Such evidence need not be direct, it may be inferred from the patentee's conduct. *See Hycor Corp. v. Schlueter Co.*, 740 F.2d 1529, 1538-39, 222 U.S.P.Q. (BNA) 553, 561-62 (Fed. Cir. 1984). Nevertheless, some evidence on the issue must exist.

Because Helena [**45] has failed to present any evidence, let alone clear and convincing evidence, that the '970 patent was procured by an applicant having withheld information through at least grossly negligent conduct, it has failed to raise a genuine issue for trial that the '970 patent is unenforceable.

E. *Helena's Other Defenses & Counterclaim*

On appeal it is Helena's burden to show not only that the district court erred, but also to persuade this court that had such error not occurred the result might have been different. *See, e.g.*, 28 U.S.C. § 2111 (1982); *Cable Elec. Prods., Inc. v. Genmark, Inc.*, 770 F.2d 1015, 1021, 226 U.S.P.Q. (BNA) 881, 884 (Fed. Cir. 1985) ("Even assuming that such errors were committed [by the district court], Cable must demonstrate that if the errors were corrected, the application of the law to the facts present would produce a different result. In short, such errors as may be demonstrated must have further been harmful.") (citations omitted); *Gardner v. TEC Sys., Inc.*, 725 F.2d 1338, 1345, 220 U.S.P.Q. (BNA) 777, 782 [**46] (Fed. Cir.) (in banc) (courts of appeal shall disregard harmless errors which do not affect parties' substantive rights), *cert. denied*, 469 U.S. 830, 83 L. Ed. 2d 60, 105 S. Ct. 116 (1984). None of Helena's other charges of error rise

to that level. The remaining "errors" concern matters on which the court made no specific rulings.

Although Helena charged SKD with unfair competition, *inter alia*, from interference with customer and vendor relationships and from patent misuse, the evidence on these matters is so inconsequential that the district court apparently did not treat it as a viable issue. Similarly, the assertion that the case should be dismissed for lack of jurisdiction based on an absence of direct evidence that Helena sold infringing products at the time SKD brought suit is meritless. Indirect evidence from which such inference may be drawn is adequate. Having reviewed the evidence called to our attention by Helena, we see no reason to remand for the district court to make specific rulings on these matters. No *prima facie* case was made out on any of them. Moreover, after the court issued its memorandum of findings of fact and conclusions of law [**47] without specific rulings, Helena failed to bring the alleged omissions to the trial court's attention. Helena's failure to give the court an opportunity to correct its alleged error in not ruling on these matters, under the circumstances here, could be deemed a waiver. Given their lack of substance, however, we are unpersuaded of prejudicial error in any event.

III

CONCLUSION

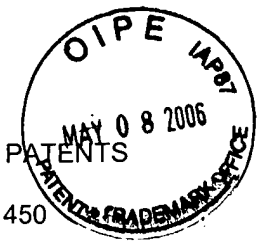
We affirm those portions of the district court's judgment holding claims 1, 2, 4, and 5 valid as between the parties, on different grounds. We also affirm that portion of the court's judgment finding that Helena's product containing lead acetate does not infringe the '970 patent. We reverse the portion of the court's judgment finding Helena's hemoglobin product noninfringing. We remand for calculation of damages.

COSTS

Each party shall bear its own costs of appeal.

MODIFIED IN PART, AFFIRMED IN PART, REVERSED IN PART, AND REMANDED

FORM PTO-1083



Docket No.: 208.1004US
Date: May 4, 2006

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450

In re application of: Lino TAVARES et al.
Serial No.: 10/045,607
Filed: October 23, 2001
For: **LORATADINE TRANSDERMAL DEVICE AND METHODS**

S i r:

Transmitted herewith is an **Response to Office Communication** in the above-identified application.

[ ] Small entity status under 37 C.F.R. 1.9 and 1.27 has been previously established.
[ ] Applicants assert small entity status under 37 C.F.R. 1.9 and 1.27.
[X] No fee for additional claims is required.
[ ] A filing fee for additional claims calculated as shown below, is required:

[X] Also transmitted herewith are:
[ ] Petition for extension under 37 C.F.R. 1.136
[X] Other: **Appellants Supplemental Brief on Appeal under 37 CFR §1.192, In Compliance with 37 CFR 41.37(c)**

[ ] Check(s) in the amount of **$0.00** is/are attached to cover:
[ ] Filing fee for additional claims under 37 C.F.R. 1.16
[ ] Petition fee for extension under 37 C.F.R. 1.136
[ ] Other:

[X] The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 50-0552.

[X] Any filing fee under 37 C.F.R. 1.16 for the presentation of additional claims which are not paid by check submitted herewith.
[X] Any patent application processing fees under 37 C.F.R. 1.17.
[X] Any petition fees for extension under 37 C.F.R. 1.136 which are not paid by check submitted herewith, and it is hereby requested that this be a petition for an automatic extension of time under 37 CFR 1.136.

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I hereby certify that this correspondence and/or documents referred to as attached therein and/or fee are being deposited with sufficient postage to the United States Postal Service as "first class mail" in an envelope addressed to " Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on May 4, 2006 .
DAVIDSON, DAVIDSON & KAPPEL, LLC

BY: _____